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An Emergent Model for Mimicking Human Neuronal Pathways in Silico

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In this study, our aim is to mimick human neuronal pathways without assuming the transition from microscopic to macroscopic scales depend upon mathematical arguments. Human neuronal pathways are natural *complex systems* in which large sets of neurons interact locally and give bottom-up rise to collective macroscopic behaviors. In this sense, correct knowledge of the synaptic effective connections between neurons is a key prerequisite for relating them to the operation of their central nervous system (CNS). However, estimating these effective connections between neurons in the human CNS poses a great challenge since direct recordings are impossible. Consequently, the network between human neurons is often expressed as a *black box* and the properties of connections between neurons are estimated using indirect methods (Türker and Powers, 2005). In indirect methods a particular receptor system is stimulated and the responses of neurons that are affected by the stimulus recorded to estimate the properties of the circuit. However, these neuronal circuits in human subjects are only estimations and their existence cannot be directly proven. Furthermore, there is no satisfactory theory on how these unknown parts of the CNS operate.

We propose a computational *emergent* model[1] that integrates the knowledge from neuroscience and *artificial self-organization* to derive from it the fundamental principles that govern CNS function and its simulation, and ultimately, to reconstruct the human CNS pathways in silico. The term *artificial self-organization* refers to a process enabling a software system to dynamically alter its internal organization (structure and functionality) during its execution time without any explicit external directing mechanism (Serugendo et al., 2011). Our *emergent* model uses temporal data collected from human subjects as an *emergent* macro-level description of the underlying neuronal pathway. Dynamic activity and spiking are modeled at the individual neuron scale. Consequently, the local information in the model is the knowledge about the behavior of individual neurons, such as generation of spikes and transmission of these spikes to their postsynaptic neurons. The effect of a spike on a target neuron is defined as a temporal membrane potential change in response to the influence of a source neuron that connects to it. That influence is not instantaneous, and is delayed by the physical distance between neurons. However, the interactions of neurons that result in macro-level *emergent* behaviors are unknown and obviously neurons alone are not able to deal with this information. Thus, we defined *adaptive* mechanisms for individual neurons based on biological knowledge. Moreover, to be able to specify purely local information about the reference macro-level pattern, we used the peristimulus frequency (PSF) analysis method (Türker and Powers, 2005).

We model the neuronal network as a dynamic directed graph $\mathcal{G}(t) = (\mathcal{N}(t), \mathcal{S}(t))$ where $\mathcal{N}(t)$ denotes the time varying *cooperative* neuron agent (vertex) set and $\mathcal{S}(t)$ denotes the time varying synapse (edge) set. The set of excitatory (resp. inhibitory) neuron agents at time t is denoted by $\mathcal{N}^+(t)$ (resp. $\mathcal{N}^-(t)$) where $\mathcal{N}(t) = \mathcal{N}^+(t) \cup \mathcal{N}^-(t)$. A synapse $\{n, m\}$ delivers spikes from n to m with a delay of d_{nm} and with a synaptic strength of η. We denote the set of postsynaptic neighbors of a neuron agent $n \in \mathcal{N}$ at time t as $Post_n(t) = \{k \in \mathcal{N}(t) | \{n, k\} \in \mathcal{S}(t)\}$ and the set of temporally closest presynaptic neighbors as $Temp_n(t)$. The nominal behavior of neuron agents is *spike firing*. The *adaptive* behaviors of neuron agents are subjected to the non-cooperative situations of the agents which are propagated by the feedbacks (Algoritm 1). We denote the set of feedbacks as $\mathcal{F}$ and we model sending a feedback $f_a \in \mathcal{F}$ using an action of the form $\mathsf{send}(f_a, \mathcal{R})$ where a is the source of f and $\mathcal{R} \subset \mathcal{N} \setminus \{a\}$ is the set of receiver agents. The *tuning behavior* of neuron agents is modelled using an action of the form $\mathsf{tune}(\{n, m\}, f)$ for $n, m \in \mathcal{N}(t)$ and $f \in \mathcal{F}$, which correspond to the adjustment of $\{n, m\}.\eta$ by f at time t. The *reorganization behaviors* of neuron agents are modeled using actions of the form $\mathsf{add}(\{n, m\})$ and $\mathsf{remove}(\{n, m\})$ for $n, m \in \mathcal{N}(t)$, which correspond to the formation and suppression (respectively) of $\{n, m\}$ at time t. The *evolution behaviors* are modelled using actions of the form $\mathsf{create}(n, m)$, $\mathsf{createInverse}(n, m)$ and $\mathsf{remove}(n)$

[1]This model has been recently reported in (Gürcan et al., 2013, 2012).

for $n, m \in \mathcal{N}(t)$. create(n, m) corresponds to the creation of a neuron agent between n and m by n having the same type of n. createInverse(n, m) corresponds to the creation of a neuron agent between n and m by n having the opposite type of n. remove(n) corresponds to the suppression of the neuron agent n by itself.

Algorithm 1 Response to the feedback f_m received at time t of neuron n where $f_m \in \mathcal{F}_{if}$ and $m, n \in \mathcal{N}(t)$.

☐ tuning condition
  if $m \in Post_n$ **then** tune$(\{n, m\}.\eta, f_m)$
☐ reorganization condition
  if $m \in Post_n$ **then**
    if $(n \in \mathcal{N}^+ \wedge f_m \downarrow) \vee (n \in \mathcal{N}^- \wedge f_m \uparrow)$ **then**
      remove$(\{n, m\})$
  else // $m \notin Post_n$
    if $(n \in \mathcal{N}^+ \wedge f_m \uparrow) \vee (n \in \mathcal{N}^- \wedge f_m \downarrow)$ **then**
      add$(\{n, m\})$
☐ evolution condition
  if $m \in Post_n$ **then**
    if $(n \in \mathcal{N}^+ \wedge f_m \uparrow) \vee (n \in \mathcal{N}^- \wedge f_m \downarrow)$ **then**
      create(Pre_n, m)
  else // $m \notin Post_n$
    if $(n \in \mathcal{N}^+ \wedge f_m \downarrow) \vee (n \in \mathcal{N}^- \wedge f_m \uparrow)$ **then**
      createInverse(Pre_n, m)
☐ propagation condition
  send$(f_m, Temp_n(t_n))$

We applied the model to the reflex responses of single motor units obtained from conscious human subjects. The exact information we used about the underlying pathways is that *sensory neurons make monosynaptic connections with the alpha motoneuron*. In this sense, we considered this path as the shortest path in the underlying network and defined its duration as l. Therefore, we initialized the simulations as $\mathcal{N}(0) = \{s, m\}$, $\mathcal{S}(0) = \{\{s, m\}, \{m, \varnothing\}\}$ and $d_{sm} = d_{m\varnothing} = l/2$ where $s, m \in \mathcal{N}^+$ and l is the latency of the estimated beginning of the pathway.

The results show that (e.g., Figure 1), **the emergent neuronal network model learns to generate what is observed in human subjects in cellular resolution**. What makes the model promising is the fact that, to the best of our knowledge, it is the first realistic model to self-wire an artificial neuronal network by efficiently combining neuroscience with artificial self-organization. Although there is no evidence yet of the model's connectivity mapping onto the human connectivity, we anticipate this model will help neuroscientists to learn much more about human neuronal networks, and could also be used for predicting hypotheses to lead future experiments.

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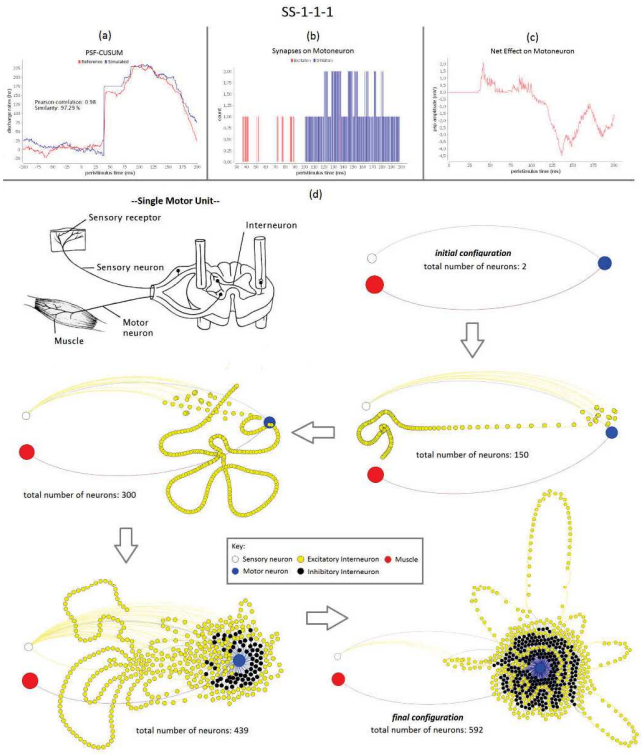

Figure 1: The results that came out of a simulation run at the end of its effort to learn the global pattern obtained from the human reflex experiment SS-1-1-1 (Gürcan et al., 2013). (a) PSF-CUSUM diagrams of the reference data (red line) and its simulated replication (blue line). Pearson-correlation of these lines is 0.98 and thus their similarity is 97.29%. (b) The temporal distribution of created excitatory (red) and inhibitory (blue) synapses on the motoneuron. (c) The net PSP on motoneuron caused by its presynaptic connections given in (b). (d) The cinematic representation of the evolution of the neural network from the initial configuration towards the final configuration together with the number and the sign of neurons. Note also that, in the final configuration, the extent of the pathways that represent the long latency reflex responses are emerging as neuronal loops.